

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/003030

International filing date (day/month/year)
22.03.2005

Priority date (day/month/year)
22.03.2004

International Patent Classification (IPC) or both national classification and IPC
A61K31/191, A61K31/18, C07D307/02, C07D311/14, C07D311/10, C07D311/08, C07D235/02, C12Q1/68,

Applicant
KARO BIO AB

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 6,7,11 (with respect to IA only)

because:

- ☒ the said international application, or the said claims Nos. 6,7,11 (with respect to IA) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|----------------|
| Novelty (N) | Yes: Claims | 11,12,15-19 |
| | No: Claims | 1-10,13,14 |
| Inventive step (IS) | Yes: Claims | |
| | No: Claims | 1-19 |
| Industrial applicability (IA) | Yes: Claims | 1-5,8-10,12-19 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 6, 7 and 11 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

D1: WO 01/36365 A

D2: WO 03/094845 A

D3: LEESON P D ET AL: "Thyroid Hormone Analogues" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 31, no. 1, 1988, pages 37-54,

Unless specified otherwise, the relevant passages are those cited in the search report.

2. Novelty (Art. 33(1) PCT)

D1 discloses compounds corresponding to formula I of claim 1, since Y or Y' can be CH and X of D1 is defined among other possibilities as S or O. Said compounds are used as thyroid receptor ligands, and can also be used in combination with other drugs such as retinoids. Claims 1-10, 13 and 14 thus lack novelty over D1 in the sense of Art. 33(2) PCT.

3. Inventive Step (Art. 33(3) PCT)

- 3.1. Claims 11 and 12, relating to the use of the claimed compounds as diagnostic agents, are not inventive in the sense of Art. 33(3) PCT for the following reason:

D1, the closest prior art, discloses said compounds as thyroid receptor ligands, but not as ligands for diagnostic purposes. The problem to be solved by claim 11 may be regarded as the preparation of diagnostic agents for thyroid-related diseases. The solutions, using compounds of formula I, is not considered to be inventive for the following reason: The use of ligands such as those of D1, for diagnostic purposes is well known in the field; as is the preparation of labelled compounds. Furthermore, document D3 discloses such a use. The subject-matter of claims 11 and 12 is thus obvious over D1 in combination with D3, without exercise of any inventive skill to solve the problem posed. The proposed solution of independent claim 11 can thus not be considered inventive.

- 3.2. Claims 15-19 relating to various combinations of the claimed compounds with other pharmaceutically active compounds are not considered to be inventive for the following reason: Since the claimed compounds are known as thyroid receptor ligands that can be combined with other compounds from what is disclosed in D1, it would be obvious for the expert in the field to combine them with other agents if deemed to be necessary, especially since the claimed combinations represent a long list of possibilities. Furthermore, D2 discloses other possible combinations corresponding to the claimed subject-matter.

It is also noted that the applicant did not claim and show support for a specific combination that would have an unexpected effect justifying an inventive activity.

4. Industrial applicability (Art. 33(4) PCT)

For the assessment of the present claims 6,7, and 11 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

5. Further objections

Claim 6 is not clear since the medical conditions to be treated are described in the

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form of a functional mechanism, i.e. disorders associated with thyroid receptor activity. The specific conditions listed in the description as well as claim 13 should be incorporated.

The same objection applies to claims 7, 8, and 11.